

REMARKS/ARGUMENTS

Reconsideration of this application in light of the above amendments is courteously solicited.

The Examiner rejected claims 1-25 under 35 U.S.C. 112, first paragraph. The Examiner's rejection is set forth on Page 2 of his office action. In response to the Examiner's rejection, Applicant attaches hereto as Exhibit A Pages 28 and 29 of the textbook entitled CLINICAL CHEMISTRY, Second Edition, published in 1994. It is clear from this text that a cellulose-based polymer such as cellulose acetate is inherently porous. The text indicates that cellulose acetate is used as a filter. Accordingly, it is clear that cellulose acetate is inherently porous. It is believed that this addresses the Examiner's issue raised under 35 U.S.C. 112, first paragraph.

The Examiner rejected claims 1-25 under 35 U.S.C. 112, second paragraph as being indefinite. Applicant by the instant amendment has amended the claims so as to overcome those objections raised by the Examiner on Pages 2-4 of his office action. Accordingly, it is respectfully submitted that all of the claims as pending comply with the formal requirements of 35 U.S.C. 112, second paragraph.

The Examiner rejected the previously submitted claims under 35 U.S.C. 103 over U.S. patent 4,214,968 either taken alone or in combination with U.S. patent 5,958,201, U.S. patent 3,691,047, and/or U.S. patent 5,958,201. As to how these rejections apply to the claims as amended herein, they are respectfully traversed.

Electrochemical sensor has two-electrode systems, i.e. working electrode and reference electrode. The working electrode sensitively responds to species of sample, but the reference electrode maintains constant potentials without responding to the species. The working

electrodes measure not values of absolute potentials, but values relative to the constant potential of the reference electrodes, that is, potential differences. Therefore, the reference electrode must maintain constant potential irrespective of surrounding conditions and return to initial equilibrium potentials after a current flow. Also, the reference electrode should be a short preconditioning time thereby being available to achieve point-of-care.

According to the present invention comprising the hydrophilic plasticizer and the lipophilic polymer, the hydrophilic plasticizer plays a role in solidifying the lipophilic polymer and absorbing water from the air to dissolve salts, thereby allowing ions to pass through the membrane. Based on these functions, the hydrophilic plasticizer activates the reference electrode and thus can shorten the preconditioning time.

According to the present invention which comprises the porous polymer and the lipophilic polymer, the porous polymer can shorten the preconditioning time, and make the inner reference electrolyte slowly flow out to maintain constant potential, thereby rendering the reference electrode being more stable for each ion of the sample.

According to the present invention as claimed, the polymeric reference electrode membrane comprises a porous polymer selected from the group consisting of cellulose acetate, cellulose acetate butylate, cellulose triacetate, nitro cellulose and a combination thereof; or comprises the hydrophilic plasticizer selected from the group consisting of glycerol, polyethylene glycol, ethylene glycol monomethyl ether, ethylene glycol, formamide and a combination thereof.

The porous polymer and the hydrophilic plasticizer of the present invention is not disclosed in Battaglia et al. 4,214,968. Cellulose acetate is disclosed in claim 4 of Battaglia et al. However, the cellulose acetate of Battaglia et al. is used not as a membrane material but as a

support, i.e. an insulation material. Also, ethylene glycol is disclosed in Battaglia et al.

However, the ethylene glycol of Battaglia et al. is used as a surfactant which improves contact between a sample and an ion-selective material (ionophore). In Battaglia et al., ionophore is an essential element and ethylene glycol cannot function without the ionophore.

In addition, the function of membrane of the present invention is different from that of Battaglia et al. According to Battaglia et al, the membrane comprises an ion-selective material (ionophore), and thus captures the ion(K^+) of sample solution, thereby sensitivity to ion increasing. Accordingly, ionophore is essential element of Battaglia et al., and cellulose acetate of Battaglia et al. functions as a material binding the ionophore.

On the other hand, according to the present invention the membrane does not comprise an ion-selective material, and thus does not capture, but rather exchange the ion(K^+) of sample solution through the membrane, thereby sensitivity to ion being constant.

According to the present invention, by applying a cellulose based porous polymer or a hydrophilic plasticizer to the membrane, the preconditioning time can be shortened, and the reference electrode becomes more stable for each ion of the sample. This feature of the present invention is not disclosed or taught by Battaglia et al.

In light of the foregoing, it is submitted that all of the claims as pending comply with the formal requirements of 35 U.S.C. 112, both first and second paragraphs, and define over the prior art of record. An early indication of allowance is respectfully requested.

An earnest and thorough attempt has been made by the undersigned to resolve the outstanding issues in this case and place same in condition for allowance. If the Examiner has any questions or feels that a telephone or personal interview would be helpful in resolving any outstanding issues which remain in this application after consideration of this amendment, the

Examiner is courteously invited to telephone the undersigned and the same would be gratefully appreciated.

It is submitted that the claims as amended herein patentably define over the art relied on by the Examiner and early allowance of same is courteously solicited.

If any fees are required in connection with this case, it is respectfully requested that they be charged to Deposit Account No. 02-0184.

Respectfully submitted,

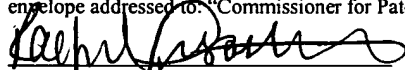
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I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: "Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313" on September 19, 2003


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torque, low-speed motors should be used. In the presence of explosive vapors, an air-driven motor should replace electrical motors. The speed of rotation of this motor and stirrer is changed by altering the air pressure.

Laboratory mixers are rated according to whether they are for continuous (8-h uninterrupted) or intermittent duty. The design of the rotating device is dictated by its intended application, such as shearing, mixing, or homogenizing. Most stirrers are made of glass, stainless steel, or Teflon. Although most mixers are intended for bench-top use, certain models are driven by 12-V DC motors and may be held by hand above the vessel in which solutions are to be mixed. Solutions in a flask may also be mixed by placing a Teflon-coated stirring bar in the flask and placing it above the stirring module that contains a rotating magnet.

Measurements on cell contents require initial preparation of the tissues. Preparation may involve grinding of the tissue in a ground glass tissue blender using manual force or a rotor driven by a simple electrical motor. For large quantities of material, a tissue blender similar to the typical kitchen blender is used to emulsify and pulverize the tissue. Several different designs of blades are available and may easily be exchanged if a different application is required. The speed at which the blades rotate is generally over 15 000 rpm.

FILTRATION

Two types of filtration are used to separate particles from liquids: *surface filtration* and *depth filtration*. *Surface filtration* (screen filtration), common in the clinical laboratory, is performed with filter papers, membranes, or sieves. The process is one of exclusion of the particles having a larger diameter than the pores of the separation medium. Surface filtration retains the solid material on the filter medium, and the filtrate passes through the filter to be collected or discarded as required. The number and size of pores can be accurately controlled in the manufacture of the separation medium so that it is possible to determine the appropriate filter for a given task.

With *depth filtration*, the thick separation medium allows particles to be retained in the body of the filter as well as on the surface. Depth filters are usually made of cotton, fiberglass, asbestos, or other materials such as diatomaceous earth. In depth filters, the matrix of fibers is usually arranged in a randomized manner to eliminate channels through the filters but to still allow passage of fluid. The lack of uniformity of the matrix does not allow the characteristics of depth filters to be defined exactly. Nevertheless, the filters can be evaluated experimentally after manufacture and a nominal performance rating assigned. Combining depth and surface filters into a single filter is useful for purifying solutions. The depth filter is used as a prefilter to trap large particles, thus lengthening the life of the secondary surface filter. Fiberglass or sintered glass is often used as a refilter for coarse materials.

Filtration may be conducted under gravity or pressure, or in a vacuum. The last may be used to accelerate the filtration rate by combining the influence of gravity, suction, and capillary attraction. The factors affecting gravity filtration include the nature of the filter medium, its surface area, and its pore size. The number and size of particles in solution and the solution's pH may also affect the filtration rate.

Many filtrations in the clinical laboratory are carried out with *filter paper*. Different types of filter paper include low-ash or ashless paper as well as various grades related to thickness. Regular filter paper leaves some ash on ignition, thus it cannot be used in gravimetric analysis. Ashless paper leaves such a low residue on ignition that its mass can be ignored. Vacuum filtration requires paper known as *hardened-grade paper*, with high wet tensile strength. Fiberglass papers have the greatest strength and combine the advantages of retention of fine particles with fast filtration. Table 1-10 describes the grade, flow rate, and retention characteristics of commonly used filter papers. *Retention* refers to the particle size of precipitate the grade will retain; *speed* refers to relative mean flow rates.

Much of the filtration in the clinical laboratories is now carried out with *membranes* of controlled pore size. These filters are made from homogeneous polymeric materials, such as polyvinylidene fluoride, cellulose esters, cellulose acetate, polytetrafluoroethylene, and polyvinyl

T A B L E 1-10. GRADE, FLOW RATE, AND RETENTION CHARACTERISTICS OF FILTER PAPERS

Grade	Thickness (mm)	Ash %	Wet Strength*	Initial Filtration Speed†(l)	Particle Size Retained (μm)
40	0.20	0.010	L	75	8
41	0.21	0.010	L	12	20-30
42	0.20	0.010	L	240	2.5
43	0.21	0.010	L	40	16
44	0.17	0.010	L	175	3
50	0.12	0.025	H	250	2.7
52	0.17	0.025	H	55	7
54	0.18	0.025	H	10	20-25
540	0.16	0.008	H	55	8
561	0.16	0.008	H	12	20-25
562	0.15	0.008	H	250	2.7

*L, Low; H, High.

†Time taken for 100 mL of clean water to pass through 15-cm quadrant folded circle, according to a modified ASTM method D881-55.

(Information from Whatman Laboratory Products, 9 Bridgewater Place, Clifton, N.J.)

chloride, depending on the intended application of the filter. The most widely used filter is composed of cellulose acetate and cellulose nitrate. The filters contain no loose fibers or particulate matter and are manufactured in a variety of sizes up to almost 30 cm in diameter and with pore sizes that vary from 10 to 0.025 μm, the latter being capable of sterilizing the filtrate by retaining microorganisms. Eighty per cent of the surface area of a typical membrane filter is occupied by pores, so that high flow rates occur through a filter even with pores of the smallest diameter. The basic structure of membrane filters is hydrophobic, although the surface of the membrane can be modified chemically to make it hydrophilic.

Membrane filters may be used under vacuum, with positive pressure, or with gravity. Some filter holders have been designed for use with syringes through which pressure is applied to filter a solution. Filters have been incorporated into certain disposable tips for use with semi-automatic pipets. These filters minimize the exchange of aerosol droplets between the tips and the pipet. This is of particular importance for DNA amplification and microbiological procedures. Other membrane filters are designed for ultrafiltration and are available with a variety of pore sizes for selective filtration. *Ultrafiltration* is a technique for removing dissolved particles using an extremely fine filter. It is used to concentrate macromolecules such as proteins, since smaller dissolved molecules pass through the filter.

Many small specimens of biological fluids may be concentrated at the same time using porous *cellulose acetate filter* cones and a centrifuge. The filter cones fit inside centrifuge tubes, and centrifugal force is used to drive water and molecules with a molecular weight of less than 50 000 through the anisotropic membrane filter. This approach is widely used to concentrate proteins in urine or cerebrospinal fluid for electrophoresis.

Fine hollow fiber filters with walls of well-defined porosity are now also used to produce ultrafiltrates or to concentrate proteins. The large filter surface allows rapid concentration.

BALANCES AND WEIGHING

Mass is an invariant property of matter. Weight is a function of mass under the influence of gravity, a relationship expressed by the equation:

$$\text{weight} = \text{mass} \times \text{gravity}$$